A Do people with certain genetic makeup have more DNA adducts than others? In other words, does the way the person handles PAH compounds vary based on their genetic makeup.

And, again, the answer is yes, there is a relationship. The way they handle PAHs varies depending on their genetic makeup.

Q And which polymorphisms do they identify as increasing the level of DNA adducts?

A It looks to me like CYP1A1 and NAT2.

Q And so the other one that they looked at, the GSTM1, was not positive for an association between that polymorphism and increased levels of adducts; is that right?

A That's correct.

Q And this study looked at 166 women who already had breast cancer; is that right?

A Yes, 166 patients. 58 percent under 50, 71 percent Caucasian. 16 percent African-Americans.

Q And what sort of women -- strike that.

Do they have a control population or were they just looking at the women who had breast cancer?

A I think there was -- no, there was no control population. They were looking at a group of patients with cancer to see if there was a difference in -- you

know, within the patient population.

Q Looking at the Discussion section, this is Page 304, they say, "The role --" this is towards the bottom of the page.

"The role of smoking in breast cancer etiology has been controversial according to epidemiological findings."

Does this study help to resolve that controversy at all?

A Yes, I think that is -- I think, that is one of the things they are pointing out.

Q They were looking for smoking-related DNA adducts; is that right?

A Right.

Q And they were looking for higher levels of women that had polymorphisms?

A Right.

Q And based on this study, the Firozi paper or other papers like this, is there any conclusion we can come to about predicting the risk of breast cancer in certain people with particular polymorphisms?

Have we gotten to that point yet or is this more of an interesting observation and we are trying to figure out what the punch line is?

A Well, I think there is no doubt that the next step here is making these tests generally available and identifying those at high risk, so that they can undergo more frequent screening and more intense screening, so early diagnosis would be possible; and you would also be able to counseling them about their higher risk of smoking or other exposures to carcinogenic agents because of their higher risk.

So I believe that as time goes on, we will probably be doing these tests as part of our evaluation of patients. Right now, it is rather expensive to do these types of tests, and it just has not caught on.

I mean, this paper was published in 2002. Usually, there is a lag between these kinds of observations and the use in the clinic, a few years at least; and it is particularly problematic because of managed care.

There is a lot more resistance to the introduction of new tests these days than there used to be because of the expense, but clearly, there is a role to be played on doing this type of testing on people. So they are aware of their risk and take steps to help protect themselves.

And it might even be possible to find antioxidants that they might be advised to take which

would help reduce the DNA damage. There might be even more specific therapies that can be given to patients who have the higher adduct levels. Attempts of reducing the exposures would, of course, be key elements to these -- these reducing the risks.

Q The idea being that someone who has this particular polymorphism should be particularly aware that they shouldn't smoke or shouldn't be exposed to higher levels of PAHs because that would increase their risk of breast cancer to a greater extent than it would someone who doesn't have those exposures?

A Right.

Q How does the Firozi paper impact your opinions with respect to Sherrie Barnes?

A Well, I think that our thinking about her is that she probably did have a greater susceptibility to damage to her DNA PAH exposure. We have no way of confirming that at this point, but the fact that she developed the cancer at a very young age -- in fact, this particular paper emphasizes younger women, premenopausal women.

I don't see that they actually looked at the difference in the different age groups but --

Q While you are looking, is it your belief that Sherrie Barnes contracted cancer at a young age is an

indication that she may have had a particular genetic polymorphism that increased her risk?
A Yes, that is what I think, but it is coupled also with a high exposure which, I think, she had as well for reasons that we've discussed before.
So that it is a combination. Again, of gene environmental interaction.
Q And the way to identify whether or not Sherrie Barnes had a particular genetic polymorphism would have been to take a blood sample when she was alive; is that right?
A Yes.
Q Let's look at the next paper. This is Gammons, G-A-M-M-O-N-S, and it is Exhibit 160. It's entitled Environmental Toxins and Breast Cancer on Long Island, I. Polycyclic Aromatic Hydrocarbon DNA adducts.
MR. PRUDHOMME: 1.
MR. HOPP: I'm sorry. 161. Yes.
(Defendants Exhibit 161 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Gammon, I think, is one of those Long Island studies. This is apart of that ongoing effort to look at breast cancer on Long Island; right?

A Yes. Yes. The authors have grown.
Q And this was published in 2002. In the Abstract at least, it says that as of 2002, the effect of PAHs on the risk of breast cancer is still not clear; is that right?
A Well, no, it says, "These data indicate that PAH-DNA adduct formation may influence breast cancer development, although the association does not appear to be dose dependent and may have a threshold effect."
One can interpret that anyway they want. It seems to me that --
Q Sure.
A It seems to me that it is supportive of the idea that I have advanced before, that the more PAH adducts you have, the higher your risk of developing a cancer and this study, I think, is consistent with that.
The fact that there was not a dose effect, I don't think is -- rules out that, that observation or that contradicts that data.
Q Okay. Looking at page -- let's see, Page 682, this is under the heading Discussion, it is just under Table 3.
A Yes.

Q In the right-hand column, it says, "In this population-based, case-control study among women on Long Island, a modest 50% elevation in the risk of breast cancer was noted in relation to the highest quintile of PAH-DNA adduct levels; however, no dose-response effect was observed."
Is that contradictory? The highest quintile means the highest 25 percent; is that right?
A Yes, that's right. Quintile actually would be the highest -- the highest 20 percent.
Q So the highest 20 percent had a modest elevation, but they don't have a dose-response effect.
Can you explain that?
A Well, you can be exposed to PAHs up to a point. And then once you've reached this critical point, then the risk -- in other words, the body's repair mechanisms are working, working, working and finally, they breakdown and you get the disease.
Q I see.
A So that would be the so-called threshold effect. It goes from 15 to 17 or whatever the numbers are.

Q The idea of being, there is no sort of trend line in the quintiles below the highest --
A That's correct. But I think that the issue here, of course, is the whole question of polymorphisms, which they didn't address.
And also, the differences in dose. In other words, what they have done is they divided them into five groups. I am trying to see -- I think, it is based upon DNA adduct levels in blood and they go on to define how they made the five groups.
Let's see. They had nondetects in 148 of the cases. You know, and then they had quintile five, that is the top 20 percent, they had 122 people in that group. Their values were over 21.9357. And I think, this is the number of adducts per ten to the eighth nucleotides.
I think, really the most important observation that needs to be made here, I think, is that you are looking at people with breast cancer already. And we talked about this earlier. DNA adducts don't necessarily stay in the body for a long time.
And I think, they were doing the lymphocytes, like we did in our case -- let me make sure that is right -- anyway, they -- I think -- I don't know if they acknowledge that, I forget. I don't know if they

acknowledged that problem here, but I think we are looking at late in the -- we are looking at ongoing exposure, basically.

And so what is going on here is that, it may be that those people, for whatever reason, had previously also higher exposure for whatever reason. But I did look at some possible sources of the PAHs. And if you look at this Table 4, a number of grilled barbecue meals in the most recent decade of life, and then poultry and fish in the most recent decade, and smoked meat, smoked poultry; and then a total of all of the PAH food intakes.

And if you look at those numbers, there does appear to be a slight tendency for the higher quintiles to have slightly more, but it is very, very little difference. So it would appear the smoking was clearly a -- also, interestingly, not terribly helpful in predicting the PAH adduct levels. It would seem to me that they missed something in terms of exposure.

Q And you think that maybe what they missed was the genetic polymorphism?

A Well, that clearly they missed. It would be important to do that because from our other study that we just looked at, you can see a big difference in the smokers, who had the polymorphism, and who didn't. And

they didn't look at that here.

Q Right.

A So, clearly, the fact that they found anything at all is probably remarkable in itself, but what is interesting is that all of the usual suspects; mainly, smoking and barbecue food.

They did not take into account, unfortunately, the other big confounder that has been discussed a lot and that is closest to a busy highway or some other environmental exposures. I don't think they ever looked at that, no.

It could well be that our high PAH people lived next to a busy highway, and therefore, get PAH exposure that way or they lived next to an industrial facility or some other thing that might be a source.

But anyway, this study clearly supports the concept that PAH adducts are associated with a higher risk of lung cancer. And it goes along with the whole concept that PAHs would cause a higher rate of mutation in cells and then increases the risk of breast cancer.

Q Let's mark this next --

A By the way, there is something interesting before we leave this paper, that should be pointed out.

Q Sure.

A That the quintile two and three almost reach

statistical significance and quintile four, which had the smallest number, dropped back down again; but clearly, the values -- first of all, they had internal control which was, you know, DNA adducts in breast cancer patients that were nondetect.

My point is that everybody who had detectable adducts had an increased risk even though it didn't reach statistical significance.

Q Which table are you on?

A On Table 2.

Q They had some breast cancer patients who were nondetect with DNA adducts?

A That's correct. And they were the controls.

Q Do you think that is realistic?

A Well, it depends on the methodology you use, but let's put it this way: In this method, these were the lowest people. So they served as controls. Whether they were truly nondetect or not, it might be that they just had a very insensitive method.

But if you look at the multivariate adjustments, anybody with adducts had a higher risk which is in itself kind of interesting. Even though they focused on the ones that had statistical significance, which is fine.

With 37 authors, many of whom are card carrying

statisticians and epidemiologists, what it really strongly looks like to me is that there is an effect. If there hadn't been an effect, just all other things being equal, some of these numbers would have to be below one in order to be having an effect.

The fact that they were all above one in itself, I think is important, but I don't think they discuss that. And I will just point that out in passing, there is a statistical thing that even though it doesn't reach statistical significant, but all of the data goes in one direction, that in itself is statistically significant.

Q So you see a trend line even though the authors indicate that they don't see a dose-response effect?

A Well, there is no dose response. There is no question about that.

But is there an association? As soon as you have detectible DNA adducts by their methodology, the risk seems to be higher. It is up by 45 percent in Quintile 2, using multivariate analysis. It is up by 48 in Quintile 3 and 1.49 in Quintile 5.

And just because the numbers were higher, because the difference between, you know, the cases and the controls in Quintile 5, it reaches statistical significance; but in Quintile 3, you are at .99 for the

lower range of the confidence interval. That is borderline. I mean, one-hundredth more and it would have been called statistically significant, if you know what I am saying.

Q Right.

A It seems to me that it showed something here that was interesting to say the least.

Q Just so we are clear on this, the issue of statistical significance at least the way it is set out in Table 2, what you are looking at is the parenthetical after the number in the last column on the right; is that correct?

A Yes.

Q And if that parenthetical, if that range of numbers includes the value one or includes the number one, then we say it is not statistically significant; is that correct?

A If it goes through one. If it goes to one, you can still be statistically significant. And if it is .99, it suddenly becomes statistically not significant using the .05 of the likelihood of it being real.

Q So the last one Quintile 5, the confidence interval is 1.00 through 2.21 and for that reason, we call it statistically significant; is that right?

A That's right. Let's go to Table 3, cases and

controls, DNA adduct levels, even though the DNA adduct difference is small, it is statistically significant with a 35 percent excess of breast cancer in those with the DNA adducts using multivariate adjustments.

Q I'm sorry. Where are you?

A First line, main effect.

Q Okay.

A In other words, using PAH-DNA adducts as a continuous variable and adjusting for the various other risk factors that are known to contribute to breast cancer, the PAH adducts were in themselves a significant contributing risk factor.

And you go down here to another finding which I considered to be important; that is, age of diagnosis. Under age 65, the patients with breast cancer and DNA adducts, the difference was statistically significant. It was a 48 percent increase in the risk of breast cancer, and it was statistically significant, 1.05 to 2.09.

Q And why is that important?

A Well, because what I had argued, I think, earlier that our patient was younger. And in this case, the younger patients had the higher risk with the PAH adduct association. Whereas the older folks, people over 65 at diagnosis, there was only an 18 percent

increase in risk.

Q What accounts for that? I mean, what mechanism or biological process would account for older people not having an increased risk than younger people having an increased risk?

A Well, I don't know, but it would seem to me that that is an observation that, you know, could be significant. What it means is that people who get high PAH exposures and have less ability to repair the PAHs due to their genetic predisposition are more likely to get cancer earlier than those who get it later.

Q It makes sense. But the bottom line here is that high DNA adduct levels correlate with risk of breast cancer Fair?

A Yes, that is correct. That is, you know, the main point of the paper.

Q The next one is 162. This is the Helmrich, H-E-L-M-R-I-C-H, paper and it is a 23-year old paper or 22-year old paper.

(Defendants' Exhibit 162 was marked for identification by the court reporter.)

THE WITNESS: Ancient history in our world.

BY MR. HOPP:

Q And it talks about Risk Factors for Breast

Cancer. How, if at all, does this paper support your opinions in this case?

MR. PRUDHOMME: Do you have an extra copy?

BY MR. HOPP:

Q I should point out that I don't think they looked at chemical exposures.

A Yes, I think I included this because we can look at the risk factors that is relevant to the history of benign breast disease, positive family history of breast cancer, Jewish religion, 12 or more years of education -- those four, yeah, were independently associated with increased risk of breast cancer.

I think our patients had benign breast disease, but no positive family history. She had one of the four. Now, there is also obesity, increases the risk. I believe Sherrie Barnes was considered to be obese. So that was a risk factor for her. She, I think, had an early age first birth. I think her youngest child -- she was fairly young.

Q 19.

A Yeah, 19, so that would reduce her risk. She was under 20. The relative risk of breast cancer drops significantly. So her having that baby, should have reduced her risk and it didn't.

Q On Page 37, they talk about Age at Menarche and

the age they use for, I guess, standard or normal is 15. That has gone down in the last 23 years; hasn't it? Now, we are talking about 12 as being --

A Well, no, it's always been 12. 15 is considered old.

Q I see.

A So what has happened in the United States in the last few years is the number of children -- girl children entering puberty has dropped significantly.

Q You mean, the age at which they enter?

A Yes, the age in which they've entered. There is a lot of six, seven, eight-year old girls now with breast development and pubic hair and underarm hair and this is causing quite a bit of concern when some of the patients require treatment. But, yeah, there is something going on in our society that is causing that.

Q So this paper is generally informative regarding nonenvironmental risk factors for breast cancer; is that right?

A That's what it was about.

Q And it doesn't look at chemical exposures at all?

A That's correct. It looks at other risk factors.

Q This is Hecht, H-E-C-H-T, deposition

Exhibit 163, entitled Tobacco Smoke Carcinogens and Breast Cancer; is that right?

(Defendants' Exhibit 163 was marked for identification by the court reporter.)

THE WITNESS: Yes, sir.

BY MR. HOPP:

Q And this is another review article; correct?

A Yes.

Q And it looks at the PAHs in cigarette smoke and their ability to cause cancer; correct?

A That's what it is talking about, yeah.

Q Now, how, if at all, does this paper support your opinions regarding Sherrie Barnes?

A Well, it discusses the evidence of PAHs and he kind of summarizes the literature focusing on some of the animal studies. And he, I think, really focuses on the fact that tobacco smoke is likely to be a risk factor here based on the potent causation of breast cancer in animal studies.

Q Okay. So he is really relying on animal studies as a mechanistic way of looking at breast cancer in humans?

A That's correct. He doesn't get very deeply into the subject on the polymorphism question, but he

does talk about the PAH-DNA adducts and breast tissue. He reviews quite a few of those papers.

Q Well, in fact, the last sentence gets to that point. He says, "In individuals in which

> The metabolism of tobacco smoke constituents to ultimate carcinogens is favored, smoking as a cause of breast cancer becomes more probable."

I mean, what we are talking about is people who have the unique ability to either metabolize or not metabolize these PAHs; is that right?

A That's right. He is alluding to that and he does talk about it a little.

Q Some sort of genetic factor?

A That's right.

Q Let me just complete the question, so we are clear for the record. There is some sort of genetic factor that affects someone's ability to metabolize the carcinogens in cigarette smoke?

A Yes.

Q And he hasn't isolated that factor, he has just simply alluded to it?

A Correct. But he has given a lot of detailed information about the animal literature. And he has referred to his own prior publication which are many.

Q Which are many or are not many?

A Are many. Six particular papers where he has written about this subject.

Q Let's look at the next one. This is deposition Exhibit 164. The lead author is Jeffy, J-E-F-F-Y. And it is entitled Epigenetics of Breast Cancer: Polycyclic Aromatic Hydrocarbons as Risk Factors.

(Defendants' Exhibit 164 was marked for identification by the court reporter.)

BY MR. HOPP:

Q Now, this is looking at BRCA-1 expression; is that right?

A That's right.

Q And tell me in layman's terms what BRCA-1 expression is.

A It is a genetic factor that predisposes people to breast cancer.

Q Okay. And one of the things he concludes is that benzo[a]pyrene disrupts the BRCA-1 gene transcription in estrogen receptor positive but not negative breast cancer cells; is that right?

A Yeah, I think -- let me just double-check that point. Benzo[a]pyrene disrupts the transcription in the receptor positive cancer cells, but not ER negative

cells.
Q Do you remember, was Sherrie Barnes' cancer ER positive or ER negative?
A It was ER positive if I recall.
Q Either way, that is reflected in the medical records, that it was an indication of whether it was positive or negative; right?
A I believe they did do that, yeah.
Q And so how, if at all, does the Jeffy paper impact your opinions with respect to Sherrie Barnes?
A Well, this author concludes that exposure to PAHs may be a predisposing factor in etiology of sporadic breast cancer by disrupting the expression of BRCA-1. So it also discusses PAHs as a risk factor of cancer. Specifically, mammary cancer and alludes to the animal data and cigarette smoke and environmental pollutants, all of which we have discussed before.
And he goes on to discuss the defective repair of the PAH-DNA adducts that causes the increase in the P53 tumor suppressor gene transversion in that gene, as he calls it, giving rise to various cancers; but I would say that the main point of this is to talk more about the BRCA protein and its -- this is I'm pretty sure this is an in vitro study.
Q This is actually a review paper?

A He says he reviews in vitro studies. Let's see what he does here. He is reviewing other people's work.
Q And that work is cell cultures?
A In vitro work, yes. That's right.
Q And tell me, we may have discussed this at an earlier point, but what is BRCA-1 transcription?
A Well, it is a gene that is associated with the breast cancer.
Q Does somebody who has that gene have a higher risk of breast cancer?
A Well, no, it is the other way around. It is, apparently, a tumor suppressor gene. And if you are deficient in that, you are more likely at risk.
And what he is saying here is that the PAHs damaged BRCA-1 expression, thus, increasing the risk of breast cancer.
Q So they interfere with the tumor suppression activity of that gene?
A Right.
Q In this in vivo studies?
A In vitro studies, that's correct.
Q I'm sorry, in vitro. And we don't know whether Sherrie Barnes had a high level or a low level of BRCA-1; is that correct?
A We don't know. That wasn't done on her as far

as I am aware.
Q Is that something that is now standard when someone is diagnosed with breast cancer? Do they look? Does a treating physician or a pathologist look for things like BRCA-1 or tumor suppressor genes or genetic polymorphisms?
A No, it is not routine as far as I know. The reason they do the estrogen receptor assay is because it, apparently, affects the treatment, but I don't think they do these other things unless they are doing a study.
Q Okay.
A They don't want it to affect therapy as far as I know.
Q Let's look at this next one. This is deposition Exhibit 165. 165 is the Li paper. L-I paper. Entitled Genetic and Environmental Determinants on Tissue Response to In Vitro Carcinogen Exposure and Risk of Breast Cancer; is that right?
(Defendants' Exhibit 165 was marked for identification by the court reporter.)
THE WITNESS: Correct.
BY MR. HOPP:
Q And this is, again, an in vitro study which

means it was conducted in petri dishes or in cell culture?
A In cell culture, right.
Q And what does Li conclude?
A That if you have a certain genetic tendency -- let's see, they talked about the CYP1B1 genotype was a significant predictor of the level of benzo[a]pyrene induced adducts in breast tissues. These observations suggest that genetic susceptibility of a carcinogenic exposure may play an important role in breast carcinogenesis.
Q So if you've got that particular polymorphism, you may have a higher risk?
A Yes. And I think -- let me see what we've got here. That the level of adducts associated with risk of breast cancer had an odds ratio of 4.38 after adjusting for confounders.
Q So it is four times higher risk if you got that polymorphism?
A Yes -- well, no -- well, if you had the adducts and the implication is that if you have the CYP1B1, you got a very high risk of cancer.
If you look at Table 2, where you got the Multiple Linear Regression Analysis of in vitro BP-induced adduct levels in breast tissue -- not at all

clear where all of that goes but --
Q Okay. But, again, the critical factor here was this particular polymorphism?
A Yes, that's right. That is what they are saying.
Q And how, if at all, does this paper impact your opinions with respect to Sherrie Barnes?
A Well, I think it is another instance of the DNA adducts from PAHs being a risk factor for breast cancer. And, you know, I think that is the point.
They are making the point which we made before that there are certain people that are more susceptible because of genetic factors. And I think that is what happened with Sherrie Barnes.
Q Okay. Let's look at the next one. It is 166. This is the Mitra paper, M-I-T-R-A, entitled Breast Cancer and Environmental Risks: Where Is the Link?
(Defendants' Exhibit 166 was marked for identification by the court reporter.)
BY MR. HOPP:
Q It is a 2004 paper looking at environmental factors; is that right?
A Yes.
Q And he puts it pretty succinctly on the first

page, the column all the way over at the right, at the bottom of the first paragraph: "So the
Question remains: Which environmental agents are cancerous and which are not?"
Right? I mean, that is the question?
A That is the question he is examining, yes.
Q And he looks at a bunch of them including electromagnetic fields and lindane, atrazine and other things that are not relevant to this case.
What, if anything, do you take away of the Mitra paper that is relevant to your opinions with respect to the plaintiffs in this case?
A Well, as we have talked about, this is a review paper. And he, you know, summarizes some of the evidence of organochlorines and PCBs. By no means does he review it all.
I don't -- you know, again, I think this is a review paper and, you know, it is interesting. He doesn't have all -- we probably could add several papers from our list here to his review so --
Q Sure.
A It is not an exhaustive review, but it is part of my practice to try to put in review papers, so we can look at all of the studies in one place.

This particular paper didn't do a particularly very good job and some papers do a better job.
Q So generally informative, but not particularly related to risk --
A That's correct.
Q And he didn't look at creosote and pentachlorophenol in isolation; right?
A No, he didn't.
Q Interestingly, he does say -- this is towards the end. This is Page 29 in the middle column -- the middle of the middle column: "Evidence
Is not conclusive about whether tobacco smoke alone could cause breast cancer."
Do you agree with that? The reason I ask is that there seems to be contradictory statements in the papers we looked at about whether tobacco smoke causes breast cancer.
MR. PRUDHOMME: Let me just interpose an objection to the form of the question. You are taking it out of context. Read the next sentence with it and I think that may answer your question.
THE WITNESS: Yes, I think the next sentence says what we have been saying all along which is in genetically predisposed people, there is probably a risk

factor.
BY MR. HOPP:
Q Okay. Sure. Let's look at this next Mitra paper. This is deposition Exhibit No. 167. We are looking at breast cancer in Mississippi. The title is Breast Cancer Incidence and Exposure to Environmental Chemicals in 82 Counties in Mississippi.
(Defendants' Exhibit 167 was marked for identification by the court reporter.)
THE WITNESS: Yeah.
BY MR. HOPP:
Q I think he gets them all.
A He has a map here of Mississippi with all the candidates with the higher rates.
MR. WINTERS: 82.
BY MR. HOPP:
Q And he does not identify Grenada County as a county with a higher rate or higher incidences of breast cancer; is that right?
A That's correct. He does not. Let's see, Grenada County is a white county and it shows no increase. The state's incidence is 58 per 100,000 in '98 and apparently, Grenada was in that level or lower.
Q How does this Mitra paper, the Breast Cancer

Incidence paper, deposition Exhibit 167, impact your opinions to the plaintiffs in this lawsuit?
A It mainly points out that if you have more environmental pollution, you have more breast cancer. And I believe that the people who live next to the Copper's facility would fit into a group of people with high levels of industrial or environmental pollution.
So this would be supportive of the general case that when you have a high pollution environment, your risk of breast cancer goes up. It is a kind of interesting ecological study because he doesn't look at any one agent. He looks at sort of the overall total pollution in a county.
And I think the reason Grenada does not show up as a county, apparently, it does not have that high a hazardous pollution index. But clearly, in my opinion anyway, the people living close to the wood treatment plant would fall into a category of high level pollution and therefore, we would fit under the rubric here of having increased risk as a result of that exposure.
Q And for his information on pollution, he looks at the U.S. EPA's air data and --
A TRI data.
Q Toxic release inventories; is that right?
A That's right.

Q So as you just said, it's overall pollution. No one pollutant or series of pollutants is evaluated; right?
A Yes.
Q Does he have relative risk data for breast cancer?
A Well, if you look at Figure 2, he has got the breast cancer incidences and the R value is 0.237 and the P valve is 0.032. So it shows a statistically significant linkage, the higher the pollution index the higher the breast cancer rate.
It goes from -- what? -- about 54 to 100 or almost 100, like 90 something. So it is almost a doubling of the risk if you look at that line.
MR. HOPP: This is deposition Exhibit 168. Exhibit 168 is the Moran paper entitled Epidemiological Factors of Cancer in California.
(Defendants' Exhibit 168 was marked for identification by the court reporter.)
BY MR. HOPP:
Q How, if at all, does a review of cancer in California impact your opinions with respect to Sherrie Barnes or the other plaintiffs in this lawsuit?
MR. PRUDHOMME: Let me just object to the scope

of the question.
MR. HOPP: Oh, I'm sorry. Sherrie Barnes. Let's keep Sherrie Barnes.
THE WITNESS: No, I think this just illustrates the point made earlier about people tend to adopt the cancer risk associated with where they live. Making an environmental factor an important point, I don't think we have any specific data that goes beyond that, and it is a very short paper.
BY MR. HOPP:
Q Let me just turn your attention to the Lifestyle section.
A Sure. Page 304?
Q Yeah, Page 304 talks about members of the Church of Jesus Christ of Latter Day Saints. That is the Mormons and then the Seventh Day Adventists, who have a lifestyle that emphasizes family life, moderation, and abstinence from tobacco, alcohol, coffee, tea and nonmedicinal drugs and he associates that with a lower overall risk of cancer; is that right?
A Yes, sir.
Q Is there support for that conclusion or that observation in other studies? Has that been looked at elsewhere?
A He gave several references here for the

observation. And it is -- I don't know -- I don't think he has got all of the references because there are, I think, other studies that found similar findings but --
Q Would you say -- I'm sorry.
A That is sort of a well-known phenomena.
Q That is generally accepted that this moderate lifestyle decreases the risk of cancer?
A That tobacco and alcohol increases the risk of cancer. There are also Seventh Day Adventists are vegetarians. So they eat less meat and less animal fat, which is a factor of increased colon cancer at least and possibly others.
Q I don't want to interrupt you.
A Go ahead.
Q So this paper, this Moran paper is generally informative, but not directly related to your opinions with regards to Sherrie Barnes; correct?
A It has to do with risk factors that are at work for cancers in general, but I think I made the point that it just makes -- certainly, lifestyle makes a difference, but they point out some other things that have to do with where you are in the world, environmental factors, and ethnic factors.
MR. PRUDHOMME: 169.
(Defendants' Exhibit 169 was marked

for identification by the court reporter.)

MR. HOPP: 169, Motykiewicz, M-O-T-Y-K-I-E-W-I-C-Z.

THE WITNESS: And guess where it is from?

MR. HOPP: I would say Poland.

MR. PRUDHOMME: Poland.

BY MR. HOPP:

Q And Motykiewicz is an in vivo study of breast tissue of a town in Poland where they had a chronic nonoccupational exposure to PAHs; is that right?

A That's correct.

Q And Motykiewicz is looking at PAH-DNA adducts in benign breast tissue as opposed to cancer patients?

A That's correct.

Q And does Motykiewicz find an association between environmental PAH exposure and higher levels of DNA adducts?

A There have been more adducts than benign cases. "Neither smoking nor genetic polymorphisms in glutathione S-transferase and cytochrome P450 influenced the levels of adducts."

Q So Motykiewicz is a negative study?

A No, I wouldn't say that.

Q Okay.

A No. What it means is, that it increases the risk of breast disease -- see, I think the problem here is that he looked at the cancerous tissue. Let me see if I read this right.

Q He is looking at intensity of staining; is that right?

A Yes. It's the staining technique.

Q So he puts the cells in a culture, and then he stains them, and he sees which cells retain the stain?

A Yes. "Samples included breast Tumor tissue from 48 breast cancer patients and benign breast tissue from 30 patients."

Cancer tissue isn't going to have PAH adducts in it. You look at the adjacent tissue not at the breast cancer tissue.

But what this guy showed is that the benign breast patients had a lot of PAH-DNA adducts -- I don't know how this paper got published, but anyway, he looked in cancer tissue where you wouldn't expect to see the adducts because it is by its very nature this rapidly reproducing tissue. That doesn't take up very much of the PAH at all once it starts its cancerous trip.

Q So you think in setting up the experiment,

Motykiewicz missed the point?

A I think he made a mistake. I think he should have looked at the adjacent normal breast tissue instead of the cancer tissue, as I have stated.

MR. PRUDHOMME: In the breast cancer patient?

THE WITNESS: Yeah, because the benign diseased patients, obviously, he was looking at tissue that wasn't cancerous. Maybe it got some fibrosis in it, but -- Another thing, if you look at the differences, it is very little difference between the two.

Relative staining intensity, I mean, it reaches statistical significance, but they are extremely close. And there is a lot of scatter in the benign disease, and he doesn't have any way of estimating exposure.

He talks about the questionnaire where they took the family history of cancer and so on, but home exposure to coal products and cigarette smoking, well, you know, some people would be much more heavily exposed than others, he doesn't really do anything to look at that.

Q So he doesn't really match up exposure with intensity of staining?

A Well, the point is that for his controls or his exposed people, it seems like what he really needed was more information on what their exposure was, whether

high exposed people for some reason environmentally.

I mean, I know in Silesia -- which I don't think this was in. I think this was in Gliwice. Silesia is across the border in Czechoslovakia. They had some of the highest PAH levels in the air and in the people that have ever been found environmentally.

So southern Poland and other areas of Poland where they have a lot of pollution -- I mean, he needs to have done something, so we know what we are looking at here and he didn't really do that.

Q So how, if at all, does the Motykiewicz paper relate to your opinions with respect to Sherrie Barnes?

A Well, I'm not sure it has much relevance, but the point is, that it was a PAH adduct paper. And, you know, he did do -- you know, he did do some looking at some of the genetic -- some of the polymorphisms as well. He looked at GSTM1, CYP1A1 and, you know, didn't find very much difference.

I don't know. I guess I included the paper because it addressed some of the issues, but I don't think it was a well-designed study, unfortunately.

MR. HOPP: Okay. We can break then and take an hour.

MR. PRUDHOMME: Sounds good to me.

(Lunch Recess.)

BY MR. HOPP:
Q Deposition Exhibit 170 is the Hoolveld paper. Did you rely on the Hoolveld paper for the purpose of formulating your opinions in this case?
(Defendants' Exhibit 170 was marked for identification by the court reporter.)
THE WITNESS: Yes.
BY MR. HOPP:
Q And what did you find significant of the Hoolveld paper for the purposes of your opinions?
A It is the study that indicates increased risk of cancer associated with TCDD exposure.
Q This is an occupational study of Dutch workers exposed to phenoxy, herbicides, chlorophenols and contaminants?
A Yes, that's correct.
Q And the main focus was TCDD? I'm sorry. It was TCDD and other polychlorinated dioxins and furans?
A Correct.
Q And there is only one death among female workers in this study; is that right?
A I think there was only 13 exposed and one death, yeah.

Q And that was from suicide?
A I don't remember but -- possibly.
Q If you look at Page 895, this is under the heading Mortality Compared With the General Population?
A Um-hmm. Right. Yes, one death of a woman was from suicide.
Q So this paper is not informative with respect to breast cancer; is that correct?
A Correct.
Q Let's look at 171. 171 is the Mallin paper, M-A-L-L-I-N, entitled Cohort Mortality Study of Capacitor Manufacturing Workers, 1944 to 2000. Did you rely on this paper for the purposes of formulating your opinions in this case?
(Defendants' Exhibit 171 was marked for identification by the court reporter.)
THE WITNESS: Yes.
BY MR. HOPP:
Q And what, if anything, is significant about the Mallin paper for the purposes of your opinions?
A Well, it shows an increased risk of cancer with the exposure of PCBs which are a dioxin-like chemical.
Q Does it show an increased risk of breast cancer or an increased risk of the incidence of breast cancer?

A No, but let me double-check. I think they didn't.
Q Look at Page 11 of 22.
A Let's see what we got here. Breasts -- basically, there is an elevated risk, but it didn't reach statistical significance. The confidence interval was 0.91 to 1.63.
Q And how many -- let's say, how many cases -- does it say how many cases of breast cancer deaths there were?
A 49 observed deaths. The important part of any study of breast cancer when you use mortality, you will tend to grossly underestimate the number of cases. Because in this era, many, many women are able to live a long, long time with breast cancer. Treatment has become relatively effective. So your mortality rate is going to be relatively small compared to the incidence rate.
Q And this study does not track incidence rates; is that correct?
A It's a mortality study. They did not study the incidences of the disease per se, only the number of people who died from those diseases as evidenced by their death certificates from the National Death Index, which also sometimes does not classify all of the

diseases that the person had.
Q So is it accurate then to say that you have criticisms of this study or are you just saying that it is limited in the amount of information it can give?
A Well, it is two factors. One is that the numbers are small, relatively small numbers. So that any -- any excess is going to be hard to detect, especially for common cancer. The more common the cancer, the larger the numbers that you need to detect an effect.
And second of all, it is a death study. It tends to underestimate the breast cancer. You don't really know much about the breast cancer prevalence because as I said, most people will respond to therapy in the modern era.
The third point is they relied on death certificates, which have been shown to be inaccurate.
And there is another point here, I believe, and that is there is a mixing. A lot of the people had short-term exposure. That is, that they included hundreds and hundreds and hundreds of people. Thousands of people. Let's see, among the workers, there is thousands of people that were -- had less than a year of exposure. And the percent of females was less time is not listed here, but there is a lot of what I would call

inaccurate estimate of dose.

In other words, there is no real surrogate of dose here. They are kind of lumping everybody together. So that what we know about work in this industry; namely, the electric capacitor manufacturing industry, is that females would be less likely to be exposed because they generally have less strenuous and less dirty jobs.

They included, I believe, employees -- let me see what they say about how they identified individuals who had exposures.

They are, basically, assuming that there were exposures in the entire area to PCBs, but there has been no further attempt to really figure out dose. So you got two things which is a number of workers who were short-term, less than a year, and usually in occupational studies, you would exclude people that had less than a year of exposure. Sometimes you use six months, but they included everybody who worked there for one minute.

Q Okay.

A And to my way of thinking, that tends to dilute the effect particularly a big chunk of your cohort is employed for less than a year.

In this case, it was 49.9 percent were employed

less than a year, which I think really reduces the value of the study. They should have excluded those folks because, you know, the likelihood that they had significant exposure and the increased risk from it is lessened. And they would be more likely to have an effect if they excluded these people.

And they also didn't make really any attempt to figure out who was heavily exposed and who wasn't. They talked about -- let's see, intervals by number of years worked, which would be a surrogate for exposure; and you know, it just -- the number of people who had worked for a long time was relatively small.

I am just looking at their Table 6 where they looked at a few specific cancers. And looking at the number of years worked, the number of males with stomach cancer, for example, that were employed for ten years or more, there were three deaths.

And naturally, it was interesting, there was a -- there was a dose response which they don't discuss. Those that were exposed for less than one year, the stomach cancer rate was 1.84, 1 to 4 years, it was 2.91, and 10 or more years, it was 3.40.

None of those were statistically significant because the numbers of each cell were extremely small, but there definitely was a gradiant. The same was true

for liver/biliary which, in fact, one of them did achieve statistical significance, those that had worked for one to four years. But, again, the number was small.

But, again, that would be another criticism that they basically didn't have a good surrogate of exposure.

Q And in addition to being a study of capacitor workers, this is also a study of Caucasian people; isn't that right?

A I think they limited it because of the nature of the workforce to those that had large numbers so --

Q So there are no non-white's in this study?

A I believe they probably -- I may -- I have to double-check to make sure that you are right. I don't know from memory that that was the case, but I will take your word for it.

Q Okay. I am going to hand you what we have marked as deposition Exhibit No. 172. 172 is the Mukerjee paper, M-U-K-E-R-J-E-E. And it is entitled Health Impact of Polychlorinated Dibenzo-p-dioxins: A Critical Review; is that correct?

(Defendants' Exhibit 172 was marked for identification by the court reporter.)

THE WITNESS: That's right.

BY MR. HOPP:

Q This is a review paper?

A Yes, it is.

Q Did you rely on this paper for the purposes of your opinions in this case?

A No. As I have indicated, the purpose of really including these is for, A, completeness and B, for example, frequently they will have some references that are important, but it does not have any new data.

As you say, it is a compilation of new data that is in the literature, but, you know, sometimes the insight that the reviewer gives can be helpful.

Q Is there anything in particular that you draw out of this paper that you find relevant for your opinions regarding Sherrie Barnes or is it just, as you say, a generally informative review paper?

A Yes, generally informative. There is one paragraph here that probably makes a point that needs to be made. I don't know if I made it before, but dioxins have a very large number of effects that are systemic poisons and they affect many, many different organs and many functions of the body.

His remark here on Page 163 in the right-hand column, in the fourth full paragraph, it says,

"The overwhelming number of toxic responses in animals to dioxins (including lethality) typically shows delay in their appearance, which supports the assumption that these responses are not the result of a direct insult from the compound."

And then it goes on to say, "TCDD is the most potent animal -- " and it goes further to discuss various defects.

So the multiplicity and the potency of the chemical to damage human beings and animals as well, I think is emphasized by this review.

Q Okay. Let's move on. The next one is 173. Deposition Exhibit 173 is the Patterson paper. It is entitled Age Specific Dioxin TEQ Reference Range.

(Defendants' Exhibit 173 was marked for identification by the court reporter.)

BY MR. HOPP:

Q Did you rely on this paper for the purpose of developing your opinions in this case?

A I don't remember from memory what was important about this paper. It makes the point the TEQs go up

with age. That is the main point of it.

Q And we talked about that before?

A We talked about that before.

Q Is there anything else particularly relevant about this paper and your opinions regarding Sherrie Barnes?

A No. I think the -- we talked about this enough already.

Q Okay. Next document is deposition Exhibit 174. Deposition Exhibit 174 is the Sterling paper, S-T-E-R-L-I-N-G, entitled Health Effects of Chlorophenol Wood preservatives on Sawmill Workers. This actually does look at pentachlorophenol exposures; is that right?

(Defendants' Exhibit 174 was marked for identification by the court reporter.)

THE WITNESS: Yes. I believe it involved some individuals who had that exposure, yes.

BY MR. HOPP:

Q Does it indicate any increase in breast cancer as a result of pentachlorophenol exposure?

A No, I think this was mostly men. I don't think there was a significant number of women. It does not even really get into cancer.

Q Does it even get into cancer at all?

A I am looking to see whether there is a notation about that. It is symptoms -- I don't see -- I don't see a discussion really of cancer.

Q Okay. To what extent did you rely on this paper for the purposes of your opinions in this case?

A Oh, I think we've talked about other health effects besides cancer.

Q Okay.

A And this class of compounds, you know, clearly has issues involving the symptoms that are described by this author: Skin, GI, neurologic, respiratory. I mean, it lists rather significant dose-related respiratory track, dermatological, systemic.

Q All right. So; this relates to other health effects, not cancer?

A That's right.

Q Next one is deposition Exhibit 175.

MR. HOPP: I only have two copies. I will give this to you when I am done.

(Defendants' Exhibit 175 was marked for identification by the court reporter.)

MR. PRUDOMME: All right.

BY MR. HOPP:

Q This is a review paper by Frederica Perera

entitled Molecular epidemiology: On the Path to Prevention?

And I may have actually marked it before, so I apologize if this is a duplicate. What, if anything -- strike that.

What, if any, relevance does this review paper have to your opinions regarding Sherrie Barnes?

A Well, Dr. Perera in this paper is making the point that if you use a more accurate biomarker of chromosomal damage, you -- and she talks about adducts and PAH adducts in particular. And some other biomarkers that are indicative of what is going to be likely an increased risk for cancer.

And she also discusses this business of polymorphism and increased risk and talks about polymorphisms and the risk of breast cancer. This is a paper back in 2000.

And so she is pointing out, you know, what had been learned up to that point on that issue. It talks about fetus and young child, susceptibility issues, and the evidence and papers that have discussed that whole problem. Where she herself has looked at PAH adducts, you know, in core blood and then looked at the risk for various other adverse health effects in the offspring correlating with the PAH adduct levels that are

detected; and then putting all of this information together to help shape preventative strategies in order to reduce risks in the future.

So her purpose here is to try to guide the public health authorities to pay attention to these markers of effect and not wait for the people to drop dead before you start taking steps to protect them.

Q This paper then, this Perera paper, deposition Exhibit 175, it is more of a policy paper really than an analysis of causation; is that right?

A Yeah, she is reviewing some of the literature on the question. And which is, again, one of the advantages of these kinds of papers is they frequently pull in references that I have not previously looked at.

Q But, again, her main emphasis is prevention of these diseases in the future as opposed to an analysis of what is causing these diseases now; right?

A Yeah, the implication of what she has been talking about is precisely what we have been talking about which is mainly if you've got exposures to PAHs and formed adducts, you are at an increased risk of adverse health affects including cancer. It's a review paper.

Q Deposition Exhibit 176, this is the Pliskova paper, P-L-I-S-K-O-V-A, entitled Deregulation of Cell

Proliferation by Polycyclic Aromatic Hydrocarbon. MFC-7 Cells Reflects Both Genotoxic and Nongenotoxic Events.

(Defendants' Exhibit 176 was marked for identification by the court reporter.)

BY MR. HOPP:

Q Did you rely on this paper for the purposes of forming your opinions?

A Yes.

Q What, if any, relevance does this paper have to your opinions regarding Sherrie Barnes?

A Well, it talks about the fact that BaP, the index PAH here, has the ability to alter cellular function by both mutagenic effects and by stimulating the Ah receptor. I think that's the major point.

Q And the authors of this paper indicate that those two particular PAHs can stimulate proliferation of human breast carcinoma MFC-7 cells at concentrations of 100 -- I am having trouble with the unit here M -- nM and higher; is that right?

This is in the Abstract.

A Nanomils (phonetic), yeah. It means that it has an effect at a low concentration.

Q 100 nanomils is a low concentration?

A Extremely low.

Q And what are human breast carcinoma MCF-7 cells?

A I think it is a cell line. I think we talked about them in an earlier paper. This is an in vitro study.

Q So she had the cells in a culture and added those PAHs; is that right?

A That's right.

Q So just a particular type of cancer cell that she was able to impact by dosing it with these compounds?

A Yeah, it showed that if you got a cancer cell, it is going to be promoted in its growth by PAHs, particularly benzo[a]pyrene.

(Telephonic interruption.)

BY MR. HOPP:

Q What, if anything, does this paper tell us about the ability of benzo[a]pyrene and benz[a]anthracene to actually cause cancer as opposed to promoting the growth of cancer cells that are already there?

A I think I had mentioned to you earlier that PAHs are both initiators and promotors. And this is a paper that discusses that promotion issue.

It is a methods paper, but it shows, you know,

the strong effect of these chemicals in doing that. And they talk about also it has a role in inhibiting apoptosis.

Q What is apoptosis again?

A It is the program cell death. It is one of the things that when a cell has a lot of changes in the DNA, the body says, oh, my goodness, this cell is not normal. So it goes over to a certain part of the genetic code and says kill it.

So the cell then undergoes an orderly disintegration as opposed to necrosis where the cell dies in a nonprogrammed method.

You know, apoptosis is thought to be an important process in preventing us all from developing cancer. All of us are exposed to these mutagens and carcinogens all of the time, but the body's repair mechanisms fix the DNA or kill the cell with the abnormal structures.

It is when these various mechanisms are overwhelmed, that you begin to have cancer. And I believe this paper indicated there was an inhibition of apoptosis.

Q Okay. So these particular PAHs -- and I know you just said this, just so I am clear, these particular PAHs interfere with the operation of apoptosis?

A Yes.
Q Next one is deposition Exhibit 177. This is the Ambrosone paper, A-M-B-R-O-S-O-N-E, entitled Cytochrome P4501A1 and Glutathione S-transferase (M1) Genetic Polymorphins and Postmenopausal Breast Cancer Risk; is that right?
(Defendants' Exhibit 177 was marked for identification by the court reporter.)
THE WITNESS: Yes.
BY MR. HOPP:
Q And she is looking at this particular polymorphism in relation to breast cancer risk in postmenopausal Caucasian women; is that right?
A Correct.
Q How, if at all, did you rely on this paper with respect to forming your opinions in this case?
A Well, I think it shows the role of the genetic predisposition issue and their interaction with the cigarette smoking. Let me see if I am correct about that.
It says here, slightly elevated risk is associated with CYP1A1 polymorphism, 1.61 and the highest for those who smoke 29-pack years odds ratio 5.22. It is similar, I think, to some of the other

papers we've looked at. When you look at certain genetic types, the risks from smoking and breast cancer become higher.
Q Sherrie Barnes was premenopausal; correct?
A Correct.
Q Next one is 178. 178 is a paper by Kogevinas, K-O-G-E-V-I-N-A-S, entitled Cancer Incidents and Mortality in Women Occupationally Exposed to Chlorophenoxy, Herbicides, Chlorophenols and Dioxins.
(Defendants' Exhibit 178 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on this paper in forming your opinions in this case?
A Well, I think this is another paper that found an excess of cancer, not breast cancer per se; but they did find for cancer overall an increased risk.
The number of women they had was very small in number. So it isn't as likely to show anything. Because small numbers, again, especially with a common disease to show an increase, it takes larger numbers usually.
Q And these are people who at least some of them worked in the production of these herbicides; is that

right?
A Yeah. Well, again, as I said before, it is not a good surrogate of exposure in this case either. They are assuming similar exposures for everybody.
Individual exposure "was reconstructed Through the use of individual job records and company records, detailed company exposure questionnaire and analyses of TCDD and other dioxin congeners in end products, reactor products, and waste streams."
"-- data on 701 female workers ever employed in production (n = 699), or spraying (n = 2)."
Q "N = 2" means that 2 people were doing the spraying?
A Yes. So it was really not --
Q So mainly production work?
A Mainly production work.
And exposure was assumed. They had a minimum of one-month of exposure. Now, again, I quarrel with such short term exposure. You tend to dilute the effect especially if you lump them together.
But anyway, they just had a small -- when you have 6, 700 people in the cohort and you have a common

disease and you don't -- they are not very old. What was the average age here? I don't think they told us.
But the number of people with 20 years since first exposure, the number of women was 2.
Q What table were you on?
A Table 2.
Q Got it.
A So even with these small numbers, you don't have -- you don't have proper latency. You need many more cases, longer termed observation.
So you really can't say anything from this study except that the numbers are tiny. And therefore, you are not surprised that they don't show much.
Q And in any event, Kogevinas did not find an increased risk of breast cancer; correct? It is on Page 549 on the right-hand column.
A That's correct.
Q This next one is deposition Exhibit 179. 179 is a paper by Bertazzi, B-E-R-T-A-Z-Z-I. We had spoken about Bertazzi.
(Defendants' Exhibit 179 was marked for identification by the court reporter.)
BY MR. HOPP:
Q He had written several papers on the Seveso

population; correct?
A Correct.
Q Did you rely on this Bertazzi paper for the purposes of your opinions in this case?
A Well, I think -- you know, historically interesting, you know, when they did this study back in the '80's -- the paper was published in '92. And they were updating the exposure.
Let's see, what did they find? Yeah, subgroup A was small, only 14 cancer cases. Zone B, liver cancer was elevated, if they lived in the area over five years, relative risk 2.8, and it was statistically significant.
Men exhibited an increase in hematologic neoplasms, relative risk 5.7, statistically significant for lymphoreticulosarcoma, which is a dioxin-related cancer in a number of other studies.
Women had an increase of multiple myeloma and myeloid leukemia. And in Zone R, soft tissue tumors in nonHodgkin's lymphoma were elevated among persons living in the area over five years. I guess, that is both women and men. Relative risk 3.5. These tumors that we just went through were elevated.
Now, breast cancer was below expectations. As we talked about, I think in the Warner paper, subsequent follow-up showed that that did not hold. There were

excesses of breast cancer in the population eventually.
A lot of these tumors that we are looking at here have shorter latencies. Particularly, the hemologic malignancies tend to have a shorter latency. Thus, I think you saw in this case, the shorter latency cancer showing up sooner.
Q In any event, Bertazzi in 1993 does not find an increased incidences of breast cancer in Zones A, B, or R; correct?
A Correct. It's interesting, however, he says there was a deficit of breast cancers in females in his summary. There was actually a 10 percent excess of breast cancer. If you look at Table 3, there was a 10 percent excess of breast cancer in Zone R.
Q Table 3, where do you see the 10 percent increase?
A Look down to breasts, look under females, see where it says 106, next to that it says 1.1.
Q That is the relative risk.
A Relative risk is 10 percent above 1.
1.1 is 10 percent elevated.
Q Okay. But the 95 percent confidence interval includes the value one?
A Right. It is not statistically significant, but as I've said, to be statistically significant --

especially since we are talking about comparisons to the general public, you know, he isn't quite right in saying there was a deficit. That is my only point.
Q Okay.
A And it was in Zone R where he had a large enough population. So he actually had a lot more cases to look at. In Zone A, they had seven cancers. Zone B, they had 36.
Remember, this study was based on data up to '86. So it was really only 10 years post lease. And as I said, you would expect certain types of cancers to occur in a shorter latency, and those were found here.
Q And breast cancer is not one of those cancers. It has a longer latency?
A It has a longer latency.
Q Let me hand you what we have marked as deposition Exhibit No. 180. This is another paper by Perera called Carcinogen-DNA Adducts in Human Breast Tissue. This is a in vitro study?
(Defendants' Exhibit 180 was marked for identification by the court reporter.)
THE WITNESS: Let's see, they used breast tissue samples. Using the p32 postlabeling method with the carcinogenic-DNA adducts, the sample include tumor

and tumor adjacent tissue from 15 women.
BY MR. HOPP:
Q Okay. So it is not in vitro. They actually extracted tissue from women and looked for adducts; is that right?
A That's right.
Q And what, if anything, do you derive from this paper for the purpose of your opinions in this case?
A That PAHs had reached the breast. That they caused adducts to form which would indicate that they would induce a higher risk of cancer in that tissue and this is a biomarker.
She does not discuss, because this is a '95 paper, the issue of polymorphism, but I think 30 percent of the folks who had the cancers, had the adducts -- I don't know if they did a control here. This was an early paper when they were just looking at it.
Five of the positive samples were from current smokers, the tissue samples from 8 nonsmokers did not show the same characteristic patterns.
Q So smokers had higher level of adducts?
A Well, it showed a certain pattern. It is called the diagonal zone of radioactivity. So she had a previous study with other tissues with exposure to tobacco smoke.

Q And what does that pattern indicate?
A Smoking basically. I mean, it is the PAHs from the cigarettes that create that pattern.
I am just trying to look here at the smoker issues. I mean, the total adducts in the nonsmokers weren't very different from the current smokers in terms of total adducts, but current smokers had more of this pattern they called a diagonal pattern there.
Q Okay. And how, if at all, is that relevant to your opinions on causation in this case?
A Well, I think it shows that smoking contributes to the -- you know, probably to the adducts, but a number of the nonsmokers had values higher -- as high or higher than the current smokers.
I mean, the highest value was in a current smoker, 8.32. And the next highest was in a former smoker and the next highest was in a never smoked so --
Q What I am having trouble with is understanding what that means to you in terms of this case?
A It means environmental exposure to PAHs reaches the breast tissue and is, I think, in this particular paper, that is really all that we found out, but we have learned more since.
Q And in this paper at least, Dr. Perera says at the end of the Abstract or at the end of the first

column of the Abstract on Page 233, that "While the Nature of the study precludes an inference of causality"; is that right?
A Yeah, she didn't have any way of looking at normal. She didn't have any way of looking at what the long-term effects was really. So she wasn't trying to say that this proved or disproved causality, correct.
Q All right. Next paper is Rohan. It's deposition Exhibit 181.
(Defendants' Exhibit 181 was marked for identification by the court reporter.)
THE WITNESS: Rohan is the second author.
BY MR. HOPP:
Q Terry, excuse me. Terry is the first author.
The title is Cigarette Smoking and the Risk of Breast Cancer in women: A Review of the Literature.
This is, obviously, then a review paper; right?
A That's correct.
Q And it looks like what he collects is animal experiments and in vitro studies; is that right?
A I think he looked at the animal studies, the in vitro studies and some of the epi studies. I think he looked at all of them.

Q And is this -- we talked about several different review papers and you stated that they are generally helpful and generally informative, but not directly relevant. Is this a particularly relevant review paper?
A No more so than the others. I mean, I think the point is that he does give us a lot of references. I mean, he had more than anybody else. He had 268. And he reviews the literature, similarly to the others. This is the 2002 update.
I think he concludes that -- in a funny way of putting it, he says, "Overall the results
Of these studies suggest that smoking probably does not decrease the risk and indeed suggests that there may be an increase breast cancer risk of smoking with long duration, smoking before the full term pregnancy, and passive smoking, but further studies are needed.
Q And then he starts off by saying, "The association between cigarette smoking and breast cancer remains unclear," right?
This is in the conclusion.

A Yeah. He doesn't really address the issue which, I think, has become crystal clear since then. That you have to adjust for the polymorphisms.
Q I'm sorry.
(Whereupon, the answer was read back as follows:
"A Yeah. He doesn't really address the issue which, I think, has become crystal clear since then. That you have to adjust for the polymorphisms.")
BY MR. HOPP:
Q You have to adjust for the polymorphisms?
A Yes, you do.
Q Let's look at Page 955. This is under the heading Epidemiological Studies of Cigarette Smoking and Benign Breast Disease. And I am looking at the second paragraph, where he says, "Women with benign Breast disease are at increased risk of developing subsequent beast cancer."
And we talked about that. That is a recognized risk factor; correct?
A Yes.
Q "However, benign breast disease

Is a heterogeneous condition consisting of many histological entities, and risk varies by histological subcategory, at least some of which might represent precursors of breast cancer."
What does that mean?
A Well, there is more than one type of benign breast disease. Now, I don't recall how -- just one minute -- Dr. Bodian, he is the one who gives the reference for that and points out that sometimes the little lumps that they feel which are judged to be benign are really carcinoma in situ.
In other words, they are precursors to breast cancer and then there are some types of fibromatous where you have multiple little nodules in the breast, he is saying that those are not necessarily precancerous.
Q Okay.
A That doesn't remove from the fact that it is an abnormality. And that it represents some kind of imbalance in the person. And that there is a general increased risk if you have benign breast disease without further class or subclassifying it.
Q Do you know did Sherrie Barnes have a history of benign breast disease?

A I don't know. I don't remember.
That is usually more commonly diagnosed in upper, middle class white women, who go to the doctor a lot. And the doctor says, you have little lumps in your breasts, but don't worry about it. It's just fibrous tissue. It's just hypertrophy. Normal breast tissue.
You know, people -- women frequently have increased lumpiness as they go through their menstrual cycle because there is estrogenic simulation of the breast tissue.
And a women who is, you know, living in rural Mississippi, is not likely to have doctors paying close attention to those things. I would find it unusual if they did comment on it.
Q Next paper is deposition Exhibit 182. It's by Rundle, R-U-N-D-L-E, et al., entitled The Relationship between Genetic Damage from Polycyclic Aromatic Hydrocarbons in Breast Tissue and Breast Cancer.
(Defendants' Exhibit 182 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on this paper for the purpose of your opinions in this case?
A I think, it is similar to a lot of the other

stuff that we have looked at. It documents that the PAHs reached the breasts. That they formed adducts and that is considered to be indicative of abnormalities in the DNA, which increases the risk for cancer. And I believe this paper is consistent with that finding as we have discussed in others.
Q Now, this was a hospital-based control study; right?
A Yeah, they did the same thing everybody else did, which is compare the normal tissue from patients who had benign breast disease and --
Q With women who had cancer?
A With the cancer patients.
Q And you identified that as a weakness of these studies?
A Yeah. In spite of that, there was a very healthy relative risk here, 4.43, showing that the odds ratio for each unit increased in the optical density score, which is, you know, the way that the DNA adducts get quantified is by their density.
Q All right. Let's look at the Abstract just briefly. This is the first column of the Abstract. He says, "Overall, neither active or passive Smoking, or dietary PAH were significantly associated with PAH-DNA

adducts or breast cancer case-control status."
So these environmental factors by themselves were not significant; is that right?
A Well, yeah, I mean, we -- I think we pointed out before that the DNA adducts in breast tissue don't seem to be terribly sensitive to smoking. Smokers and nonsmokers seem to have levels that are very similar.
The only environmental factor that they took into account was diet, I think, and, again, that has not been shown to be very powerful either.
Let me just see -- they controlled for -- well, I wouldn't take the time now to find it what they controlled for, but they controlled for confounders as they put it, and still found a big difference between the cases and the controls.
Q And what he was saying at least in the Abstract, was that it was this genetic susceptibility that plays a role in breast cancer as opposed to the environmental exposures?
A No, I don't think that is what he is saying. I think what he is saying is individuals that can't clear the PAHs properly are at increased risk, but it is an interaction with a gene and the environment.
Q Okay. I understand that.

And how does he identify genetic susceptibility? Is it just increased levels of DNA adducts that indicates that someone has a genetic susceptibility or does he identify some particular genetic defect or polymorphism?

A I don't think he did any genetic testing. I think he assumed within a higher PAH-DNA level, that they had a genetic tendency in that direction.

I don't see any discussion of measurement of -- he says here that -- this is on Page 1286, right-hand column, in the first paragraph that starts on the next column over, but "The finding reported here

> That, after controlling for two of the major PAH exposure sources (tobacco smoke and diet), PAH-DNA adducts levels in tumor tissue were positively associated with case-control status, might suggest that interindividual variation in metabolic and/or DNA repair pathways plays an important role in breast cancer."

Basically, we are saying that the people that don't clear the DNA properly are the ones who are at greater risk.

Q So if you are collecting adducts and not clearing them, he assumes there is a genetic reason for that?

A Yes. And now, he says there is a second reason which is progressive changes in tumor cells lead to greater formation of adducts and tumor tissue, but he looked at adjacent nontumor tissue and found that there was also the same increase. And so I don't know why he is bringing that up.

Q Our next exhibit is Exhibit 183. It is another Rundle paper. This is entitled Molecular Epidemiologic Studies of Polycyclic Aromatic Hydrocarbons-DNA Adducts and Breast Cancer.

(Defendants' Exhibit 183 was marked for identification by the court reporter.)

BY MR. HOPP:

Q And this is 2002. It's two years later than the one that we just looked at deposition Exhibit No. 180?

A Right.

Q Deposition Exhibit 182. Is this a review paper?

A Actually, this is a review paper and there is actually new data in here.

Q What question is Rundle trying to answer in this paper, deposition Exhibit 183?

A He reviews our studies on the role of PAH-DNA adducts and breast cancer. Additionally, the report on the analysis of the reliability of the scoring method using immunohistochemical assays and potential bias arising from benign breast disease as controls.

Q Did you rely on this paper for the purpose of formulating your opinions?

A Yes, I think that it does certainly contribute to our understanding of how PAHs would increase the risk of breast cancer.

Q How does it contribute to our understanding?

A Well, it just further underscores the DNA adducts in the breast tissue and how it affects -- you know, its presence in the cancer tissues.

It also talks about the susceptibility issue. They measured one of the genotypes, the GSTM1 null genotype, that is associated with increased adduct levels showing that certain people had more adducts and they identified at least one of the genetic factors were.

They also talked about how there is a fairly high reliability of their assay. However, technician quality significantly contributed to the variability.

Thus, indicating that the test has to be done very carefully by a highly skilled person, which is a technique point.

And they talked about the use of benign breast disease would tend to overestimate the prevalence of family history of breast cancer compared to that of healthy controls.

In other words, they, I think, would support the notion and it would probably be better to use nonbreast -- don't use benign breast disease for controls.

Q Well, in fact, he talks about that in the Discussion section, this is on Page 204.

A Um-hmm.

Q He says, "Our data show that

> Increased levels of PAH-DNA adducts in breast tissue are associated with breast cancer case-control status, although with our modest sample size, this finding is only statistically significant when adducts levels in tumor tissue are compared to those seen in benign tissue."

A Yes, I know.

Q How is that --

A Well, it reached statistical significance -- the difference was very small, but because of the small numbers, it didn't reached statistical significance, but it was elevated in both tumor and nontumor tissue.

But then, again, he had small numbers here. I mean, that is part of the reason why he did not get statistical significance.

MR. HOPP: I'm sorry. I need to take this. Can we take a short break?

MR. PRUDOMME: Sure.

(Brief Recess.)

BY MR. HOPP:

Q Dr. Dahlgren, again, going back to deposition Exhibit 183, the 2002 Rundle paper, at the end, it is right above the references, this is Page 26, I believe, he repeats something that you have been saying.

His analysis of the "GSTM1 polymorphism Indicate that the polymorphism plays an important role in adduct formation in cases but not controls."

A That is what he says.

Q So that supports your opinion that people with this genetic polymorphism are more susceptible to the induction of cancer as a result of exposure of PAHs?

A That's right.

Q And forgive me if I have asked you this, but has the role of genetic polymorphism and the incidences of cancer been studied for polychlorinated dioxins or furans?

A Yeah, we had looked at some. We had one paper on that.

Q One paper?

A Relatively little compared to a lot more has been done with the PAHs and the dioxins. And clearly, we should start looking at that because it is likely to be an extremely important factor.

We are learning more and more about the gene environment interaction. And as we do more studies, it is a powerfully important point.

Q Let's look at the next one and this is deposition Exhibit No. 184. This is the Saintot paper, S-A-I-N-T-O-T. And this is another paper that looks at the Interaction Between Genetic Polymorphism of Cytochrome P450-1B1 and Environmental Pollutants in Breast Cancer Risk.

(Defendants' Exhibit 184 was marked for identification by the court reporter.)

MR. HOPP: I'm sorry. I don't have an extra copy, Keith?

MR. PRUDOMME: No problem.

BY MR. HOPP:

Q And these are women who live near a waste incinerator?

A That's right.

Q And living near a waste incinerator was a surrogate for exposure; correct?

A That's right.

Q And he found that the women who carried this particular polymorphism the Val CYP1B1 allele had a higher risk; is that right?

A Yes.

Q And what is the word allele mean?

A That refers to a certain part of the geno. It's a section of the genetic code.

Q It is just another way of characterizing this polymorphism?

THE WITNESS: You gave me two.

MR. HOPP: I'm sorry.

THE WITNESS: That is just another word that is referring to gene.

BY MR. HOPP:

Q Looking at the top of Page 184, top of the right-hand column, all of the women in this study were white; is that right?

A I will take your word for it. This was a French paper; wasn't it? So many non-white's in France. Probably.

Q It says, "All women were white." It is in the right-hand column.

A I don't see it right away, but I believe you.

Q Okay. Do we know whether Sherrie Barnes had this particular polymorphism the one that is discussed in the Saintot paper?

A No, I don't.

Q Other than generally indicating that people with this particular polymorphism are at a greater risk for cancer as a result of exposure to PAHs, how does this paper affect your opinions with respect to Sherrie Barnes?

A Well, as you know, waste incinerators put out dioxins and dioxin-like compounds. So what they are talking about here is an increased breast cancer risk from dioxin exposure and that those who have the increased susceptibility indeed do develop a higher prevalence of the breast cancer.

Q So this gets to what we were just talking about, so this is a paper that looks at a surrogate of TCDD exposure and a genetic susceptibility?

A Correct.

Q We've talked about different types of polymorphisms; right? I mean, the CYP1B1 is different in some way from some of the other polymorphisms we looked at; is that right?
A Yes.
Q How many different polymorphisms are there?
A Many. The reason they pick these -- in this case, that particular enzyme -- they say here in the paper is induced by dioxins. So you expect to see more of that particular enzyme if you were exposed to dioxin and what they also go on to say is that, that would then increase the production of toxic intermediates, which is what we were talking about earlier.
Q Well, when we say, "polymorphisms," what does it mean in layman's terms?
A Genetic variation. Polymorphism just means that your hair is brown and her is light blond. You know, that is determined by genetic factors. And the color of your eyes, your skin, you know, a lot of your characteristics are as a result of slight differences in the genes.
Q But the polymorphisms that we have been talking about in these papers all have these alphanumeric labels attached to them. Is there a list of these that have been identified by geneticists or someone else?

Is there a Table I could go to somewhere to find a list of identified genetic polymorphisms?
A Yes. You could probably find a review paper that would list -- see, this CYP1B1 is an enzyme system in the liver and in other cells. That metabolizes things and what they are doing is they are looking at the gene that controls or turns on and off the production of that protein.
Q Okay.
MR. PRUDOMME: That enzyme.
THE WITNESS: Well, the enzyme is the protein. In this case, protein is functioning as an enzyme. Proteins can do other things. They can be signaling proteins. They can be inhibiting proteins, stimulating proteins, all kinds of proteins, but one of the proteins in this case is a CYP1B1 enzyme which is part of the cytochrome P450 system that we talked about.
It is those enzymes when they are stimulated, it alters the way the body handles stuff coming through. So they hypothesized that this would be an important point where these type of chemicals are exerting an effect and they found an effect.
It's not that they started -- it says here, "We hypothesized that polymorphism of CYP1B1 may contribute to the

interindividual susceptibility to environmental procarcinogens in relation to breast cancer risk." And they found that this was indeed the case.
Q Sure. So when they pick which polymorphism to study, they are looking for ones that they already know have a particular effect in the metabolism of these substances; is that right?
A Yes. A couple of these other papers have looked at that same enzyme system and the same genetic control.
Q Right. The next one is deposition Exhibit 185, this is a paper by Shi, S-H-I, et al., entitled Reduced DNA Repair of Benzo[a]pyrene Diol Epoxide-Induced Adducts and Common XPD Polymorphisms in Breast Cancer Patients.
(Defendants' Exhibit 185 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on this paper for the purpose of forming your opinions?
A Yes, I think this also makes the point about PAHs damaging DNA and that the DNA repair mechanisms are

inhibited by the damaged genes from the benzo[a]pyrene, active metabolite. They also looked at the benzo[a]pyrene diol epoxide, BPDE.
So they were looking at the metabolite -- the toxic metabolite of benzo[a]pyrene. And they were doing this in vitro. They took peripheral blood lymphocytes from female breast cancer patients and then they showed that the DNA repair in these patients with breast cancer was ineffective or less effective.
Q This is the first paper that I have ever seen which somehow ranks or rates DNA repair capacity. It shows a DNA repair capacity level; is that right?
A Yes. And it is, apparently, this -- there is two common polymorphisms that are linked in this DNA repair and they list them there, the XPD polymorphisms and then they list the two, which I won't go through because they are very long.
We found that the mean DNA repair level was significantly lower in breast cancer patients than controls. And they had a three-fold increase in risk for breast cancer than those with the higher DRC after adjustment for age, smoking, and assay-related variables.
Q But this gets to a point that you were making earlier, and that is that we are all exposed to these

carcinogens on a daily basis and the reason we don't all drop dead from cancer is that we have -- or don't drop dead from cancer right now.
A Yes, or die from it.
Q Is because we have DNA repair mechanisms?
A Absolutely.
Q And the people who get cancer often have less effective DNA repair mechanisms?
A Exactly.
Q Do you know anything about Sherrie Barnes' level -- strike that.
Do you know anything about Sherrie Barnes' DRC level as identified about in this paper?
A No, we did not have the opportunity to have done that study.
Q But we can say -- strike that.
Is it your opinion, though, based on the fact that she died fairly young of cancer that she had some sort of a defective or less effective DNA repair capacity?
A I would hypothesize that that probably would be part of her increased susceptibility, yes.
Q Let me hand you deposition Exhibit 186. 186 is a paper by Tang, T-A-N-G, et al.
(Defendants' Exhibit 186 was marked

for identification by the court reporter.)
MR. PRUDOMME: Don't tell me I have two of them? No, it is two different papers.
MR. HOPP: Actually --
THE WITNESS: Rundle, it has two papers attached for some reason.
MR. HOPP: We already marked that. I don't know why -- my apologies.
THE WITNESS: Well, the third author of this is Rundle. So it is the same group.
BY MR. HOPP:
Q And also, Dr. Phillips is an author on this paper as well; right?
A Yes.
Q And Dr. Phillips is the scientist who did the DNA adduct study in this case?
A That's correct.
Q And in this -- well, let's identify it. This is deposition Exhibit 186 and it is by Tang, et al., entitled Polymorphisms in the DNA Repair Enzyme XPD are Associated with Increased Levels of PAH-DNA Adducts in a Case-Control Study of Breast Cancer.
And this is along the lines of what we have just been discussing; is that right?

A That's correct.
Q Again, they are looking at the ability of the DNA to repair itself and how that relates to the breast cancer incidence or breast cancer risks; is that correct?
A That's right.
Q And the conclusion is that XPD polymorphisms -- let's look at it. Page 165, they say, "Our Data do not support the hypothesis that XPD polymorphisms play a role in the etiology of breast cancer"; is that right?
A Where are you reading from?
Q This is Page 165 above the References. The sentence beginning with "Our data do not support." It is right after Footnote 8.
A Well, but the next sentence says, "However, diminished XPD-mediated DNA repair capacity does appear to be associated with increased DNA damage in tumor tissue. To the extent that increases in DNA damage may lead to further mutations and contribute to genetic instability in the tumor. XPD may play a role in genetic

susceptibility to tumor progression."
Q What does that mean? I mean, they say that the polymorphisms itself does not play a role, but then there is some sort of XPD-mediated DNA repair capacity issue?
A Yeah, what they are saying is, that if you are deficient in this repair mechanism and for whatever reason you get cancer, you are less able to modify the progression of the cancerous process.
In some people, DNA repair can reverse even fairly late changes in DNA and other cellular systems that promote or cause cancer to occur.
In this case, the deficiency of repair appears to be post-initiation and more important in the progression issues and that is what these words mean.
Q And we don't know whether Sherrie Barnes had this XPD polymorphism; do we?
A No.
Q Next one is deposition Exhibit 187.
(Defendants' Exhibit 187 was marked for identification by the court reporter.)
MR. WINTERS: I get one now.
BY MR. HOPP:
Q 187 is another paper by Tang and Andrew Rundle,

entitled Sulfotransferase 1A1 (SULT1A1) polymorphism, PAH-DNA Adduct Levels in Breast Tissue and Breast Cancer Risk in a Case-Control Study.

Again, this is a paper that looked at another particular type of polymorphism; is that right?

A Yes.

Q And what did the authors conclude?

A That this polymorphism is associated with breast cancer risk. In other words, they looked at some controls, found that the people who had this particular polymorphism had a higher risk of breast cancer.

Q Well, look at the Summary, doesn't it say, "Contrary to our hypothesis, PAH-DNA adduct levels in breast tissue were not associated with the SULT1A1 genotype"?

A Correct. But they --

Q Sorry. Go ahead.

A No, go ahead.

Q It seems to conflict with what you just said. Am I misunderstanding the paper?

A I am reading the final sentence. You read the next to the final sentence. They had information or data that supported both of those statements.

Q Okay. So it says, "Our findings are

Consistent with a prior report that the Arg/His polymorphism in SULT1A1 is associated with breast cancer risk"?

A In other words, there is no -- you don't get an increased risk of adduct levels with this polymorphism, but you do get an increased risk of breast cancer.

Q Okay.

A So some other mechanism is at work here.

Q Got it. Just having this polymorphism increases your risk of breast cancer?

A That's right.

Q But the mechanism is not the increased collection of DNA adducts?

A Yes, that is what it says.

Q And we don't know whether Sherrie Barnes had this particular genotype; correct?

A Correct.

Q And this particular polymorphism; right?

A That's correct.

Q The next one is deposition Exhibit 188. This is probably the oldest paper that we have looked at, 1977.

It's a Williams, et al., paper, entitled Association of Cancer Site and Type with Occupation and

Industry From the Third National Cancer Survey Interview; is that right?

(Defendants' Exhibit 188 was marked for identification by the court reporter.)

THE WITNESS: Yes.

BY MR. HOPP:

Q And they looked at over 7,500 cases of cancer and I guess, did interviews to try to find out what sort of exposures they had; is that right?

A Yes.

Q And in this case, breast cancer is associated -- I am looking at major findings. This is on Page 1148. It says, "Breast cancer was

More common among women who were teachers, other professionals, and among those working in banking, real estate, accounting, and insurance."

Do you see that?

A Yes.

Q What, if anything, do you derive from a paper like this?

A Well, this is just, again, a risk factor paper. And that the breast cancer risks are associated with higher social economic status. Similar to what we had

talked about in that other 1983 paper. I think it was '83 -- '85, something like that, where we talked about the various risk factors.

Q All right. So just to the extent to which this impacts your opinions, it is that higher social economic standing is a higher risk of breast cancer?

A Right.

Q And one of the other things they talked about is cancer of the prostate is more common among ministers, farmers, plumbers, and rubber workers?

A What are the links between those?

Q Yeah. I mean, this is really just an observation that may or may not be an indication of some sort of --

A Well, these kinds of studies are very useful for getting clues about where to go to do more detailed studies of exposures and so on.

Back in the '70's, this was a very popular thing to do. It has become less popular because of the -- relationships tend to be hard to track down.

Q Our methods have gotten more sophisticated in terms of identifying exposures?

A We are more interested in getting some estimate of what the exposure even if it is a surrogate exposure, but we need to have more information about exposure so

we can understand its association.
It is clearly being upper, middle class, white women raising your risk. It doesn't necessarily tell you why unless you look and see what upper, middle class, white women have in common. I suppose one of them is that they get more medical care. They may take more medicines. They may get more estrogens. They may take more birth control pills. They may be more sedentary. They may go to the hairdresser more often. They may use more chemicals in their cosmetics.
There is a whole host of hypotheses one can generate as to why that social economic group has more breast cancer, but I think that would be what you would do. You would go ahead and look at some of those variables and rather than looking at their occupation.
Q Sure. Let's look at deposition Exhibit 189 is a paper by Xiong. I guess, X-I-O-N-G --
(Defendants' Exhibit 189 was marked for identification by the court reporter.)
THE WITNESS: Yes.
BY MR. HOPP:
Q -- and others. Entitled Sensitivity to Benzo[a]pyrene Diol-Epoxide Associated with Risk of Breast Cancer in Young Women and Modulation by

Glutathione S-transferase Polymorphisms: A Case-Control Study.
Is this another look at polymorphisms and their effect on breast cancer issues?
A Yes, it is.
Q And what is the authors' conclusion?
A Well, if you are more sensitive to BPDE-induced chromosomal changes, you are more likely to get cancer. And they talked about genetic, environmental factors interacting and they basically found that -- let's see, the polymorphism, the risk was -- they had the GSTT1 null variant, that was deficient in that glutathione pathway, the risk was increased eight-fold, and it was statistically significant.
So that is another polymorphism that we did not focus. We did have some earlier -- this morning, we did talk about some glutathione pathways that are deficient the same as they have shown here.
Q And we don't know whether Sherrie Barnes had that particular polymorphism?
A No, we don't.
Q What is sensitivity to BPDE-induced chromosomal aberrations?
A Well, they incubated the patients' lymphocytes with this toxic of metabolite benzo[a]pyrene and they

induced more chromosomal breaks in the breast cancer patients than in the normal controls.
Q What does that mean?
A That means they were less able to repair the deficit problems. It is the same kind of thing we were looking at in some of these other studies.
Q They extracted tissue from women who had breast cancer?
A Yes.
Q And then they put it in a culture and added this toxogen to see what the effect was; right?
A Right.
Q And the effect was that the cells were not able to break down the -- were not able to metabolize the toxogen; right?
A No. No.
Q What happened?
A What happened was they got more chromosomal breaks in the cancer patients than they induced in the noncancer patients. And if they were less able to withstand or repair -- it is probably more likely less able to repair the damage induced by the benzo[a]pyrene diol-epoxide.
Q So the cells were not able to fix themselves?
A Right. It was a three-fold difference.

Q And again, looking at Results, this is on deposition Exhibit 183 -- I'm sorry, 189.
A And it was more profound in the younger people, the women who were under 45 years of age, suggesting that the earlier breast cancers were even less able to fix the chromosomal breaks.
Q Looking at the Results paragraph, this is Page 8466. Greater than 80 percent of the subjects were Caucasians in both cases and controls; is that right?
It is about 10 or 12 sentences down under Results.
A Yeah, 80 percent were Caucasian.
Q Handing you what we have marked as deposition Exhibit 190. Deposition Exhibit 190 appears to be a -- something from the News section of the Journal of the National Cancer Institute. It is not actually an article more kind of a information --
(Defendants' Exhibit 190 was marked for identification by the court reporter.)
THE WITNESS: -- a news piece --
BY MR. HOPP:
Q -- a news piece.
What was the purpose of citing this piece? For what purpose did you use it in formulating your

opinions?
A I don't remember why I included this. You might want to drop it. It doesn't have any information in it that is particularly useful.
Q Okay. Let's move onto 191. 191 is a paper by Kennedy, et al., entitled DNA Repair Capacity of Lymphoblastoid Cell Lines from Sisters Discordant for Breast Cancer.
(Defendants' Exhibit 191 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on this paper for the purpose of formulating your opinions in this case?
A Let's see, I think this is another one of those genetic polymorphism, genetic predispositions due to poor DNA repair and they used another technique.
They exposed patients to the benzo[a]pyrene metabolite using lymph cells from the patients and 158 cancer patients and 154 control sisters.
And there was a difference in the DNA repair between the sisters. The ones with cases had 8.6 times -- I guess, an aggregate of 8.6 times less capacity that could repair than their nonbreast cancer sisters.

Q Again, they had some way of measuring DNA repair capacity; is that right?
A Yes.
Q How do they do that?
A The difference between staining immediately after treatment, minus that after four hours of repair, divided by the initial damage -- so it was using an immunofluorescence technique looking at the benzo[a]pyrene DNA adducts and they looked at them initially, and then they looked at them in four hours.
And the normal or the sisters without the breast cancer were able to fix more of the defects and remove more of the staining as opposed to the cancer patients, who were less able to make the repairs.
Q And what was the purpose of studying pairs of sisters? I mean, how does that strengthen --
A Well, what they are really playing out here is that even sisters do not have the same necessary polymorphism.
I am a little surprised that there was so much difference between sisters, but anyway, that is what they -- they used the sisters for controls because they were pretty good controls. I don't know whether they went ahead and discussed whether this was a post or precancerous effect.

They are saying that measuring this DNA repair would be an important thing to do to try to identify high risk individuals before they develop cancer.
So it is an interesting study from that point of view. It further underscores this whole issue of the importance of DNA repair and probably reflects some different -- they didn't do any gene studies in this paper. So we don't know what genes is associated with this particular repair problem.
Q It is kind of a -- it is not a precise from that standpoint; that is, we don't know why the gene is repairing themselves, we just know that the staining is different after four hours and that is an indication of increased DNA repair?
A Right.
Q Now, Sherrie Barnes has both half sisters and full sisters; right?
A Right.
Q But isn't this an indication that even testing DNA repair capacity or polymorphisms in her sisters, wouldn't particularly be indicative of her level of DNA repair capacity or her particular polymorphism?
A You have to repeat the question.
Q I will try again.
Doesn't this paper; that is, the Kennedy paper,

indicate that you wouldn't be able to learn much about Sherrie Barnes' DNA repair capacity or her particular polymorphisms even if you were to take a blood sample from one of her sisters?
A Yes, that's correct. But what I don't think they have addressed is the issue of whether or not this may be a consequence of some type of significant exposure that had poisoned the DNA repair mechanism. We talked about that earlier.
How possibly the exposure of PAHs can effect the ability of the cells to repair themselves. So this may not be a genetic deficit, it may be an acquired deficit.
Q But the Kennedy paper does not answer that question?
A No, it does not.
Q In fact, the Kennedy paper does not look at any sort of toxic exposure?
A No, it doesn't. It is just looking at the whole issue. If the DNA repair is impaired, you are more likely to have breast cancer.
This is almost kind of like a methods paper, but it illustrates a powerful point, the importance of repair.
Q I mean, it is a fairly obvious point. If your

DNA cannot repair itself, you are more likely to have problems that may result in the breakdown of your DNA?
A Absolutely.
Q But this is an experimental proof of that hypothesis?
A That's correct. It also had our friend Motykiewicz as one of the authors.
Q A better paper from our friend from Poland.
A Yes.
Q Let's look at the next one. This is Kriek, K-R-E-I-K, deposition Exhibit 192. This paper is titled Polycyclic Aromatic Hydrocarbon-DNA Adducts in Humans: Relevance as Biomarkers for Exposure and Cancer Risk.
(Defendants' Exhibit 192 was marked for identification by the court reporter.)
BY MR. HOPP:
Q This is a review paper; is that right?
A Yes.
Q And one of their conclusions is that "Breast cancer patients were found to have significantly higher PAH-DNA adduct levels in breast tissue than did non-cancer controls."
I am looking at Page 227.

MR. PRUDOMME: Do you have an extra copy?
MR. HOPP: I'm sorry.
MR. PRUDOMME: Page 197?
MR. HOPP: Page 227.
THE WITNESS: Okay. What part of that page were you focusing on?
BY MR. HOPP:
Q I have to find it. Right above concluding Remarks:
"Breast cancer patients were found to have significantly higher PAH-DNA adduct levels in breast tissue than did non-cancer controls."
A That is what it says.
Q And this is a 1998 paper and they are more -- we have seen since 1998 --
A We have seen a lot more papers.
Q And a lot more papers on that same subject and in fact, a lot more refined papers?
A That's correct.
Q More precise papers?
A Yeah, getting more and more information about what was going on. '98 in the scientific world is a long time ago.
Q Well, in fact, this study of DNA repair and

polymorphisms is rapidly changing even now or even rapidly developing right now?
A Oh, yeah. We are getting more sophisticated in what we are looking at.
Q Now, it identifies -- this paper, the Kriek paper, identifies in the Methods section, several different ways of looking at PAH-DNA adducts?
A Right.
Q Including both p32 postlabeling and competitive ELISA, E-L-I-S-A?
A Yes.
Q Is there a consensus -- and then there are other methods that are identified?
A Um-hmm.
Q Different types of chromatography?
A Right.
Q Is there a consensus with respect to what is the fastest or the most precise way to identify PAH-DNA adducts?
A Well, the p-32 postlabeling technique seems to be the most common. Most of the papers we have looked at subsequent to this one used that technique.
And they in this paper -- let's see what they say. I forgot -- yeah, they just say that the quantification has become accurate and overall the

methodology for DNA adducts in humans have become more reliable, detects background carcinogen adduct levels in environmentally exposed persons. Particularly combinations of the various methods now enable us to elicit specific adduct structures with the detection limit of one adduct and ten to the eighth unmodified nucleotides are even lower.
So it really doesn't make a judgment about which one to use, but as I say, subsequent studies seen most commonly to use a p32-postlabeling technique.
Q On Page 217, they talk about a problem with the p32-postlabeling. It says, "Quantification is a major concern of the p32-postlabeling technique. Adduct recoveries are variable, and relatively minor changes in the procedures may introduce large differences in the reported adduct values."
Do you see that?
A I don't see it, but I know that is true.
Q They do go on to talk about within the same laboratory, there is some consistency. And I think I can actually cite a paper from Dr. Phillips on this point.

A Yeah, and I think what I said before in the earlier part of this deposition, was that Dr. Phillips uses this -- the technique that I told you about, which is that he runs the exposed and the controls at the same time without knowing which is which; and you know, all of the variables then are going to be the same, so that you can compare the two.

You can't compare one run and one lab using the absolute numbers because of this variability question. But if you run the samples together, you can get reliable results.

Q Is it accurate to say that this is really more of a methods paper than anything else?

A Well, you could say that they are talking about methodology, but they also looked at some patients. They looked at -- how many people did they look at?

I thought they looked at some groups of workers. They don't give a reference. Maybe it is a review paper in terms of data.

Q In their Concluding Remarks, they are talking about "The quantification of PAH-DNA Adducts in human tissues and cells has been achieved with a number of highly sensitive techniques" and he goes on and list them.

A Right.

Q And further on in the Concluding Remarks, "Overall, we conclude that the methodology applied for DNA adducts in humans has become more reliable in recent years, allowing to detect even background carcinogen adduct levels in environmentally exposed persons."

A Yeah, I read that sentence already. You're right. There is no data in here. It is just a review paper.

Q A review paper of methods?

A That's right.

Q Next one is deposition Exhibit 190 --

A No, 193.

Q 193. This is a paper by Spitz, S-P-I-T-Z, et al, entitled Genetic Susceptibility to Cancer.

(Defendants' Exhibit 193 was marked for identification by the court reporter.)

BY MR. HOPP:

Q Did you rely on this paper for the purpose of your opinions in this case?

A Well, this is a review paper. Also, this talks about policy and it makes some of the same points that

we have already made.

Q So generally informative but not particularly related to causation; correct?

A Yes.

Q Next one is deposition Exhibit 194. This is stowers, S-T-O-W-E-R-S, et al., 1985. Again, in our world, a fairly old paper; right?

(Defendants' Exhibit 194 was marked for identification by the court reporter.)

THE WITNESS: Yes.

BY MR. HOPP:

Q And they are looking at the formation and persistence of benzo[a]pyrene metabolite-DNA adducts in animals; is that right? This is actually a review of animal studies.

A Yes, it looks at a number of specific adducts in various tissues in benzo[a]pyrene treated animals. Basically, this is trying to, you know, understand what happens to benzo[a]pyrene when it gets inside the body. And then they also want to know how long it stays, turn overrates, and the accumulation of adducts from long-term exposures to low levels.

And it talks about noncancer effects due to these DNA problems. So it is an interesting paper even

though it is 20 years old because they actually do experiments or refer to experiments, that let us understand why long-term, low level exposure is capable of causing significant disease.

And I think if you look at the design of this study, they actually did four PAHs.

Q Okay.

A And then they looked at the levels in various tissues and then talked about the means and standard deviations of those adducts and picomole per milligram of DNA, which is an older way of expressing the data.

Q How, if at all, does this paper relate to your opinions regarding Sherrie Barnes?

A Well, it demonstrates the persistence in the tissues of these carcinogenic PAHs. It shows how they don't go away when they get into the tissues, they can continue to cause an adverse effect.

They didn't specifically look at the breast tissue, but we know from the other papers that these metabolites and PAHs do get into the breast tissue.

And these authors are simply pointing out that when you see these DNA adducts in the tissues, you can expect both cancer and other noncancer health effects. And they talk about repair and the importance of repair also.

Q Okay. So generally informative but not particularly related to causation; fair?
A Well, it is generally informative of the causation issue of PAH damaging the DNA and leading to cellular dysfunction.
Q In animals?
A In animal studies, yes.
Q Deposition Exhibit 195, this is the Veglia paper, V-E-G-L-I-A, entitled Bulky DNA Adducts and Risk of Cancer: A Meta-analysis.
(Defendants' Exhibit 195 was marked for identification by the court reporter.)
BY MR. HOPP:
Q We've talked about this before. A meta-analysis combines the data from several different studies and tries to come to a more powerful conclusion?
A Well, putting together several studies, they get more power to see effects. So, in this case, they looked at DNA adducts and they looked at, apparently, seven articles that met their criteria. And five had to do with lung cancer, one oral cancer, and one bladder cancer.
Q So no breast cancer in this paper?
A That's correct.

Q And what was their conclusion based on their meta-analysis of these other papers?
A Meta-analysis shows that current smokers of high levels of adducts have an increased risk of lung and bladder cancers.
Q They talk about -- this is towards the end of the paper, on Page 159. They talk about publication bias.
"Publication bias could justify the findings if small positive studies have greater chances of being published than small negative studies."
Have you ever run into that before? Have you ever heard that notion before?
A I've heard it. If someone goes through all of the trouble to do the study and even if it is negative, they will probably publish it, but I mean, there are negative studies. We have looked at them ourselves here today.
But it is said that there is some tendency to not publish negative results. Again, I don't know of any evidence to support that, but it is talked about a lot.
Q Okay. The next paper is by Dao, D-A-O.

Deposition Exhibit 196 is the Dao paper. It is entitled Carcinogenesis of Mammary Gland in Rats.
(Defendants' Exhibit 196 was marked for identification by the court reporter.)
BY MR. HOPP:
Q And this is -- it is a very long paper. What is it? I mean, what does it do? How does it help you?
A Well, I believe that this is a study that reviews the various chemicals that induce breast cancer in rats.
And he starts off with hormones. Then they go on to the polycyclic aromatic hydrocarbons and they don't seem to go -- at least in the first page into some of the others, but it is mainly looking at the PAHs it looks like.
Q This is 1964; is that right?
A Yup.
Q So how does this paper either support or detract from your opinions regarding Sherrie Barnes?
A It supports the fact that PAHs induce breast cancer.
Q All right. In animals?
A In animals.
MR. HOPP: Can we take five minutes?

THE WITNESS: Um-hmm.
(Defendants' Exhibit 197 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Dr. Dahlgren, our next exhibit is 187. I'm sorry, 197. This is Davis, et al. It is entitled Medical Hypothesis: Xenoestrogens As Preventable Causes of Breast Cancer. And it is a 1993 paper.
Did you rely on this paper for the purposes of formulating your opinions in this case?
A It is a review paper. It talks about PCBs, polycyclic aromatic hydrocarbons. It really kind of alludes to some of the additive effects.
In other words, if you were to look at the additive effects -- in other words, they have got a figure here in Figure 1, where they are talking about various ways that breast cancer can be promoted and induced.
I would just say it is like the other review papers. It's a little bit old. So it is probably not as thorough as some of our later papers, but it touches on the issues of environmental causes of breast cancer.
It points out that it is not likely that these things are unrelated. So, I guess, I would say that it

add to, you know, our body of literature.
Q Okay. But this paper itself; that is, the Davis paper, does not identify any relative risks for breast cancer based on any particular type of exposure; right?
A It reviews studies where it gives relative risk, but it doesn't have any of its own data.
Q I am looking at Page 375, under the heading Hypothesis and the authors say, "In light of the pivotal role of estrogen, we hypothesize that exposure to some xenoestrogens elevates endogenous hormone levels especially -- " it looks like 16 alpha-OHE1 "-- which stimulate breast cell proliferation and thereby induce or promote breast cancer."
What is xenoestrogen?
A A estrogen from outside, not a naturally occurring one. For example, we talked about PCBs and PAHs as having an estrogenic effect stimulating the estrogen receptor. Those are xenobiotic.
Q And what is endogenous hormones?
A That is the naturally occurring hormone. In this case, estradiol, which would be made by the body.

Q Okay. So they are saying that these artificial estrogens elevate the level of natural hormones in the body?
A Well, they can. Yes, they can stimulate the endogenous hormone levels by various mechanisms.
Q And what is -- I have seen the term in some other papers and we may see this as we continue. I have seen the term exogenous estrogen.
What is an exogenous estrogen as opposed to endogenous estrogen?
A The same as the xenobiotic. It is an estrogen or estrogen-like compound that is from outside the body. Exogenous meaning outside.
Q In the years since 1993, in the 12 years that this paper has been published, there has been some work done to try to determine whether exogenous -- in the years since 1993, there has been studies conducted to try to determine whether the hypothesis we see on Page 375 is accurate or not; is that right?
A I don't recall that we've run across papers that have looked at endogenous hormones.
There are studies with dioxin thyroid hormones where they showed the thyroid hormone is inhibited. And there is some competitive activity with thyroid hormone and they mention endogenous.

(Telephonic interruption.)
THE WITNESS: You were asking a question about has anybody done measurements since then of endogenous estrogen and specifically looking at this 16 alpha-OHE1, this is a endogenous hormone that stimulates breast production.
BY MR. HOPP:
Q Okay. And the answer is?
A The answer is I didn't run across a study where they had done that. I mentioned that the thyroid hormone has been studied, but I don't recall seeing endogenous estrogen levels or some of these other hormones having been looked at, I just don't recall offhand seeing that.
These authors are suggesting that be done and this is actually looking at this issue of women that have children early in life are at lower risk -- I'm sorry. They are saying that if you have children earlier in life and had more of them, they have higher risk of breast cancer, which is an opposite of what I was looking at elsewhere.
Anyway, they are hypothesizing a mechanism which has not been pursued as far as I am aware.
Q Okay. Next one is deposition Exhibit 198. It is by Wolff, Mary Wolff. It is entitled Pesticides-How

Research Has Succeeded and Failed in Informing Policy: DDT and the Link with Breast Cancer.
(Defendants' Exhibit 198 was marked for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on this article for the purpose of forming your opinions in this case?
A Well, this is another review article. Although, Dr. Wolff has published herself the original paper that linked DDT and breast cancer.
In this paper, she is just reviewing the work that has been done and I think it has the same mechanism as many of the other review papers.
It gives us some information, but it does not give us any basic data on which to base the opinion. It is just a review paper.
Q As indicated in the title, a lot of her focus on this is based on policy; is that right?
A Yes. And I think maybe the reason why this paper is here is because she makes the point, the rates of breast cancer -- this is on the last page in the last paragraph; Page 90.
Q Okay.
A "Rates of breast cancer

Occurrence in the United States have steadily risen since 1940. During that same period, pesticides and PCB residues in human adipose tissue in the United States have shown parallel increase, following their introduction into commerce around the time of World War II. Since then, despite much research on the question, only three factors have been generally agreed to be strongly linked to breast cancer: Age, country of birth and family history. These factors are not readily amenable to change. Medicine has done its job well in finding new avenues of treatment and detection. However, the existence of a cure without a cause continues because no pathways for prevention have been found."

So she is expressing frustration.

Q She says a little earlier on -- this is, again, on the last page, on the far left column, first full paragraph.

"Existing methodologies are often inadequate to study complex diseases like cancer, reproductive dysfunction and neurotoxicity, especially when attempting to link subtle biological effects with complex and low-level exposures."

Do you agree with that statement?

A Yes, but I think what is really going on now with our better understanding of genetic predisposition, and our ability to measure things like adducts and measure DNA repair and all of these other things that we talked about over the last several hours.

See, she wrote this paper back in '95. And, you know, in the last 10 years, a lot has happened. Partially because of her efforts. I mean, she has pushed the agenda rather sharply forward. And so, I mean, her frustration here has been listened to.

Q Our next one is deposition Exhibit 199. This is by Payne, P-A-Y-N-E, et al., and the title is Mixtures of Four Organochlorines Enhance Human Breast Cancer Cell Proliferation; is that right?

(Defendants' Exhibit 199 was marked for identification by the court reporter.)

THE WITNESS: Yup.

BY MR. HOPP:

Q What type of study is this? Is this a --

A It is an in vitro study.

Q So, again, cells in cultures; is that right?

A That's right.

Q And what is Payne and his co-authors studying?

A The effect of four of the organochlorines and how they interact with each other. And, you know, they looked at the single agent and they looked at various combinations to see whether there was synergy or additive effects.

Q Okay. And the names of the organochlorines are spelled out in the Abstract? They are pretty long.

A That's right.

Q And none of them are TCDDs?

A That's right.

Q And none of them are the organochlorines that we commonly see in pentachlorophenol; is that right?

A That's correct. This is the old DDT -- hexachlorocyclohexane and the -- yeah, DDT, hexachlorocyclohexane.

Q By DDT, you mean the pesticides that now has been banned; is that right?

A Yes.

Q And what is Payne conclude?

A They are an additive. They didn't find a synergistic effect.

Q So by "additive," you mean one plus one equals two as opposed to synergy where one plus one equals --

MR. PRUDOMME: -- three or four or five.

THE WITNESS: Correct. There is no evidence of synergy.

BY MR. HOPP:

Q What else do you take from this paper in terms of your opinions regarding Sherrie Barnes?

A Well, the main thing is this is one of the few papers that actually tries to look at the effect of two things together. So I thought it would be useful to include it.

To point out when you have more than one agent, you are going to have a greater effect if they are all work towards the same end point. Anyway, in this case -- in this case, a proliferation or stimulation of breast cancer cells.

Q All right. The next exhibit is deposition Exhibit 200. This is a paper by Li, L-I, entitled Aromatic DNA Adducts in Adjacent Tissues of Breast Cancer Patients: Clues to Breast Cancer Etiology.

(Defendants' Exhibit 200 was marked

for identification by the court reporter.)
BY MR. HOPP:
Q Did you rely on the Li paper for the purposes of your opinions in this case?
A Well, yes, I think this contributes to our understanding of the fact that carcinogenic DNA adducts in breast tissue, in this case aromatic DNA adducts, which usually refers to PAHs, that these do -- are associated with a higher risk of developing breast cancer.
And they talk about it in terms of "Findings support the hypothesis that environmental carcinogenic exposure in addition to cigarette smoking may be associated with the etiology of human breast cancer."
Q And do they find support for that hypothesis?
A Yes.
Q Now, in terms of the methods for this paper, they took cells from women who are undergoing mastectomies; is that right?
A Yes, they took some surgical specimens of normal human breast tissue from breast cancer patients and compared them to 29 noncancer patients undergoing

reduction mammoplasty.
Q All right. So this paper does not have the problem we identified earlier where the controls were people with benign breast disease?
A Right.
Q These were just women who were having reduction surgery?
A Correct.
Q And what they found was that the DNA adduct levels in tissues adjacent to the cancer -- strike that.
What they found was "the total Adduct levels were significantly higher in normal adjacent tissues of breast cancer patients than those in normal breast tissues of noncancer controls."
A Right.
Q Do they identify the cause of those higher DNA levels?
A No, but their main point is that it occurred in nonsmokers. They are saying smoking is one source of PAHs, but there is also environmental PAH exposure, which is contributing to the PAH-DNA adducts. So they are, basically, saying there is environmental exposure which is playing a role in breast cancer.

Q But they have not identified the sources of those environmental exposures; is that right?
A They do not. They did not find where they were being exposed, but they point out benzo[a]pyrene and other PAHs is a ubiquitous environmental pollutant. So, basically, it is your food and polluted air and so on.
Q Our next one is deposition Exhibit 201, I believe, right?
(Defendants' Exhibit 201 was marked for identification by the court reporter.)
MR. PRUDOMME: 201.
BY MR. HOPP:
Q This is a paper by Linda Birnbaum entitled Developmental Effects of Dioxin and Related Endocrine Related Chemicals, 1995; is that right?
A Yes, it is.
Q Now, who is Linda Birnbaum? What is her --
A She is the -- I believe, the head now at least of the Health Effects Research Lab at USEPA.
Q She is actually a fairly influential in terms of setting policy about dioxin and studies of dioxins in cancers?
A Yes, she has written a great deal about the subject and she is very persuasive. And she is a

very -- a very knowledgeable individual in this area. Yes.
Q And what is the emphasis of this paper deposition Exhibit 201? What is the point she is trying to make?
A Well, she points out that TCDD and its related dioxin-like compounds have a variety of toxic effects. And that the focus here is their effects on hormones in the body.
And she points out because it affects all of the different endocrine systems to one degree or another, it is likely to have an adverse effect on development. And that development could include such things as cancer in the future.
In other words, if your DNA is damaged or your other developmental pieces our damaged in utero or in early childhood, that could affect your risk for other effects like cancer and developmental effects as well, like brain function.
She is, I think, focusing quite a bit on the developmental effects and how that affects not only reproduction but neurobehavioral end points.
Q This is a review paper; is that right?
A It is.
Q And she is not really talking about breast